

## **AMENDMENTS TO THE CLAIMS**

This listing replaces all prior versions and listings of claims in this application.

### **Listing of Claims**

1. (Withdrawn) A human artificial chromosome vector comprising a fragment of human chromosome 21 or a fragment of human chromosome 14 from which the distal region of the long arm and/or the distal region of the short arm has been deleted.
2. (Withdrawn) The human artificial chromosome vector according to claim 1, wherein the fragment of human chromosome 21 or the fragment of human chromosome 14 is of about 2-16 Mb.
3. (Withdrawn) The human artificial chromosome vector according to claim 1 or 2, wherein the distal region of the long arm of human chromosome 21 is deleted within the 21q11 region.
4. (Withdrawn) The human artificial chromosome vector according to claim 3, wherein the distal region of the long arm of human chromosome 21 is deleted at AL163204.
5. (Withdrawn) The human artificial chromosome vector according to claim 1 or 2, wherein the distal region of the short arm of human chromosome 21 is deleted within the 21p region.
6. (Withdrawn) The human artificial chromosome vector according to claim 5, wherein the distal region of the short arm of human chromosome 21 is deleted at AL163201.
7. (Withdrawn) The human artificial chromosome vector according to claim 1 or 2, wherein the distal region of the long arm of human chromosome 14 is deleted within the 14q region.
8. (Withdrawn) The human artificial chromosome vector according to claim 7, wherein the distal region of the long arm of human chromosome 14 is deleted at AL157858 or AL512310.

9. (Withdrawn) The human artificial chromosome vector according to claim 1 or 2, wherein the distal region of the short arm of human chromosome 14 is deleted within the 14p region.

10. (Withdrawn) The human artificial chromosome vector according to claim 9, wherein the distal region of the short arm of human chromosome 14 is deleted at at least one position selected from the group consisting of OR4H12, OR4Q4, RNR2, OR4L1, RNU6C, FDPSL3, K12T, C14orf57, OR6S1, M195, OR4K14, MGC27165, LCH, OR10G3, OR4K3, OR4E2, H1RNA, ATP5C2, OR11H6 and OR4M1.

11. (Withdrawn) The human artificial chromosome vector according to any one of claims 1-10, wherein a recognition site for a site-specific recombination enzyme is inserted into the proximal region of the long arm and/or the proximal region of the short arm of human chromosome 21 or human chromosome 14.

12. (Withdrawn) The human artificial chromosome vector according to claim 11, wherein the site-specific recombination enzyme is Cre enzyme.

13. (Withdrawn) The human artificial chromosome vector according to claim 11 or 12, wherein the recognition site for the site-specific recombination enzyme is the loxP sequence.

14. (Withdrawn) The human artificial chromosome vector according to any one of claims 11-13, wherein the recognition site for the site-specific recombination enzyme is inserted into AL163203 in the proximal region of the long arm of human chromosome 21.

15. (Withdrawn) The human artificial chromosome vector according to any one of claims 11-13, wherein the recognition site for the site-specific recombination enzyme is inserted into a more proximal position than the deletion site of AL157858 or AL512310 in the proximal region of the long arm of human chromosome 14.

16. (Withdrawn) The human artificial chromosome vector according to any one of claims 11-13, wherein the recognition site for the site-specific recombination enzyme is inserted into a more proximal position than the deletion site within the 14p12 region in the proximal region of the short arm of human chromosome 14.

17. (Withdrawn) The human artificial chromosome vector according to any one of claims 1-16, wherein the deletion of the distal region of the long arm and/or the distal region of the short arm is by substitution with an artificial telomere sequence.

18. (Currently Amended) A method for producing a human artificial chromosome vector, comprising the steps of:

(a) obtaining cells that retain human chromosome 21 ~~or human chromosome 14~~;

(b) deleting a distal region within the 21q11 region of the long arm and/or a distal region within the 21p11 region of the short arm of the human chromosome 21 ~~or human chromosome 14~~; and

(c) inserting a recognition site for a site-specific recombination enzyme into a proximal region of the long arm and/or a proximal region of the short arm of the human chromosome 21 ~~or human chromosome 14~~.

19. (Cancelled)

20. (Currently Amended) The method of claim ~~19~~ 18, wherein the cells ~~with high homologous recombination efficiency are derived from~~ chicken DT40 cells.

21. (Currently Amended) The method of ~~any one of claims 18-20~~ of claim 18, wherein in step (b) the deletion of the distal region within the 21q11 region of the long arm and/or the distal region within the 21p11 region of the short arm is by substitution with an artificial telomere sequence.

22. (Currently Amended) The method of ~~any one of claims 18-21~~ of claim 18, wherein in step (b) the distal region within the 21q11 region of the long arm of human chromosome 21 is deleted at AL163204.

23. (Withdrawn and Currently Amended) The method of ~~any one of claims 18-21~~ claim 18, wherein in step (b) the distal region within the 21p11 region of the short arm of human chromosome 21 is deleted at ~~AL163204~~.

24.-25. (Cancelled)

26. (Currently Amended) The method of ~~any one of claims 18-25~~ of claim 18, wherein in step (c) the site-specific recombination enzyme is Cre enzyme.

27. (Currently Amended) The method of ~~any one of claims 18-26~~ claim 18, wherein in step (c) the recognition site for the site-specific recombination enzyme is the loxP sequence.

28. (Currently Amended) The method of ~~any one of claims 18-27~~ claim 18, wherein the recognition site for the site-specific recombination enzyme is inserted into AL163203 in the proximal region of the long arm of human chromosome 21.

29.-32. (Cancelled)

33. (Currently Amended) The method of ~~producing a human artificial chromosome vector comprising foreign DNA~~ claim 18, further comprising, ~~in the method according to any one of claims 18-30~~, the step of:

(d) inserting foreign DNA into human chromosome 21 ~~or human chromosome 14~~ in the presence of a site-specific recombination enzyme.

34.-36. (Cancelled)

37. (Currently Amended) A method of introducing foreign DNA into a recipient cell, comprising the steps of:

- (a) obtaining donor cells that retain human chromosome 21 ~~or human chromosome 14~~;
- (b) deleting a distal region within the 21q11 region of the long arm and/or a distal region within the 21p11 region of the short arm of the human chromosome 21 ~~or human chromosome 14~~;
- (c) inserting a recognition site for a site-specific recombination enzyme into a proximal region of the long arm and/or a proximal region of the short arm of the human chromosome 21 ~~or human chromosome 14~~;
- (d) inserting foreign DNA into the human chromosome 21 ~~or human chromosome 14~~ in the presence of a site-specific recombination enzyme;
- (e) preparing microcells from the donor cells that retain the human chromosome 21 ~~or human chromosome 14~~;
- (f) fusing the microcells and recipient cells; and
- (g) confirming the introduction of the foreign DNA into the fused recipient cells.

38. (Original) The method of claim 37, wherein the recipient cell is an animal cell.

39. (Original) The method of claim 38, wherein the animal cell is a mammalian cell.

40. (Currently Amended) The method of ~~any one of claims 37-39~~ claim 37, wherein the recipient cell is a pluripotent cell.

41. (Original) The method of claim 40, wherein the pluripotent cell is an embryonic stem cell (ES cell), or a mesenchymal stem cell or a tissue stem/precursor cell.

42. (Currently Amended) A method of producing a cell that expresses foreign DNA, comprising the steps of:

- (a) obtaining donor cells that retain human chromosome 21 ~~or human chromosome 14~~;

- (b) deleting a distal region within the 21q11 region of the long arm and/or a distal region within the 21p11 region of the short arm of the human chromosome 21 ~~or human chromosome 14~~;
- (c) inserting a recognition site for a site-specific recombination enzyme into a proximal region of the long arm and/or a proximal region of the short arm of the human chromosome 21 ~~or human chromosome 14~~;
- (d) inserting foreign DNA into the human chromosome 21 ~~or human chromosome 14~~ in the presence of a site-specific recombination enzyme;
- (e) preparing microcells from the donor cells that retain the human chromosome 21 ~~or human chromosome 14~~;
- (f) fusing the microcells and recipient cells; and
- (g) selecting cells expressing the foreign DNA among the fused recipient cells.

43. (Original) The method of claim 42, wherein the recipient cell is an animal cell.

44. (Original) The method of claim 43, wherein the animal cell is a mammalian cell.

45. (Currently Amended) The method of ~~any one of claims 42-44~~ claim 42, wherein the recipient cell is a pluripotent cell.

46. (Previously Presented) The method of claim 45, wherein the pluripotent cell is an embryonic stem cell (ES cell), or a mesenchymal stem cell or a tissue stem/precursor cell.

47.-48. (Canceled)

49. (New) A method for producing a human artificial chromosome vector, comprising the steps of:

- (a) obtaining cells that retain human chromosome 21;
- (b) deleting a distal region of the long arm and/or a distal region of the short arm of the human chromosome 21 to produce a human artificial chromosome vector that does not have a telomere side of AL163204 of the long arm and/or a telomere side of AL163201 of the short arm of the human chromosome 21; and
- (c) inserting a recognition site for a site-specific recombination enzyme into a proximal region of the long arm and/or a proximal region of the short arm of the human artificial chromosome vector.

50. (New) The method of claim 18, wherein the distal region within the 21q11 region of the long arm comprises AL163204 and the centromere side of the long arm of the human chromosome 21.

51. (New) The method of claim 18, wherein the distal region within the 21p11 region of the short arm comprises AL163201 and the centromere side of the short arm of the human chromosome 21.